CLINICAL SYMPOSIUM

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Ulcerative Colitis

Medical Management

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ULCERATIVE colitis varies greatly in severity. It may be mild, with involvement of only the rectum and rectosigmoid, so that general treatment alone may be sufficient to bring about recovery or at least remission. Or it may be severe and fulminating, with septic fever, severe anorexia, dehydration, and great blood loss due to almost constant bloody diarrhea. In this stage, management of allergic reactions is not practicable, the psychiatrist may do more harm than good, and ileostomy may cause death.

Treatment in general is best divided into two parts, that which consists of palliative and supportive measures, and that designed to affect more directly the inflammatory reaction in the bowel.

Under supportive treatment, which I think is the most important part of therapy in the average case, we might consider, first, control of malnutrition. It is important to make the diet as liberal as possible in order to get adequate calories for the patient. For years, a high protein diet has been stressed. The patients often have hypoproteinemia and usually have nitrogen deficiency. In many cases it may be necessary to supplement the diet by protein hydrolysates orally and intravenously.

Supplemental vitamins are essential because of poor absorption, loss in diarrheal content, and inadequate intake. Vitamins should be given in large doses by mouth and, if there is marked evidence of avitaminosis, parenterally also. In addition to the ordinary synthetic vitamins, brewer's yeast should be given by mouth as a source of natural vitamin B complex. If vitamins are given parenterally, in addition to vitamin C and vitamin B complex, liver extract is also beneficial.

Correction of the depletion of blood and blood proteins is important. As there is usually anemia due to loss of blood as well as hypoproteinemia, transfusions of blood and plasma should be used freely.

Another palliative measure of importance is control of diarrhea. The diet should be smooth and low in residue to avoid stimulating intestinal motility. Inert substances such as bismuth and kaolin which have a tendency to retard motility and solidify stools may be given. Tannalbin also is frequently used for this purpose. Tincture of opium is occasionally beneficial if used for only a short period of time in an acute flare-up. (It should not be used for long periods, however, because of the tendency to habituation.) Bed rest, sedatives and antispasmodics are helpful in controlling diarrhea, and removal of foci of infection also may help.

Psychotherapy is of definite value as a palliative measure. Although it is desirable to have a formal psychiatric evaluation, this is not always feasible. In any event, general psychotherapy will fall largely on the shoulders of the attending physician, who should, of course, administer psychotherapy to the limit of his ability. Very often he can accomplish much by patient listening, sympathetic understanding, reassurance, helping the patient adjust to this serious chronic disease, helping him with emotional and family problems. (Problems associated with a dominating parent are found commonly in patients having this disease.)

Palliative treatment alone may induce a remission in some of the mild cases. In considering the measures which are supposed to attack more directly the inflammatory reaction in the colon, one may mention, first, vaccines and serums.

For many years Bargen has claimed that a diplostreptococcus is the specific causative agent in most cases of ulcerative colitis. Bargen's work has not received general confirmation. It is felt by most workers that the streptococcus described by Bargen is a variant of the streptococcus fecalis, and there is no real evidence that it is other than a secondary invader. For that reason the use of diplostreptococcus antiserum and vaccine is confined largely to Bargen and his associates.

Serums such as polyvalent anti-bacillary dysentery serum, which was first advocated by Hurst in England and used in this country by Crohn and by Bockus, are not used much now. I have seen a few patients, in whom the disease was acute, respond rather strikingly to this serum. It was the opinion of Bockus, and I think also of Crohn, that the benefit was not due to a specific effect but rather the result of a foreign protein reaction. It is noteworthy that the patients who do have a definite or striking response are usually the patients who develop rather severe serum sickness. Serums and vaccines are very little used since the advent of chemotherapy and antibiotics.

Block and Pollard summarized their experience and the experience of others regarding sulfonamides and antibiotics in the treatment of ulcerative colitis about as follows: The sulfonamides, although definitely helpful as a therapeutic adjunct in the treatment of ulcerative colitis, are definitely not curative

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in this disease. The response is variable and unpredictable; it may be rather striking at times, and at others there is no apparent benefit. Benefit from sulfonamides is probably due to their effect on secondary infection and on the bacterial flora of the fecal material. The investigators believe the most effective sulfonamide is sulfathalidine, with sulfasuxidine a close second. The locally acting sulfonamides may be given over a long period of time in small doses in order to maintain remission; this cannot be done so well with the more completely absorbed sulfonamides. However, in patients with infection and fever, and perhaps complications of ulcerative colitis, the sulfonamides, such as sulfadiazine, which act after system absorption, may be more valuable than the locally acting drugs.

Penicillin given parenterally has been found to be of very little if any value in inducing remission in the average case of ulcerative colitis. It may be very valuable, however, as adjunct therapy in some of the acute febrile complications such as pericolic abscesses. The effectiveness of penicillin given orally, as advocated by Streicher, requires further evaluation. Essentially the same thing can be said of streptomycin. It has not yet been clearly evaluated but seems to have little or no value in inducing remission. The principal effect of streptomycin is probably on the intestinal flora, an effect which can be achieved more easily and certainly more economically by use of sulfonamides. The rapid development of resistance by the coliform organisms to streptomycin would seem to make it of doubtful value in the average case of ulcerative colitis. However, it too has been found rather helpful at times in conjunction with other measures to combat acute complications with fever in this disease.

Among other measures supposed to affect directly the inflammation of the bowel is antiamebic therapy. This is of course of no value unless amebic infection is present. In an occasional case, when the appearance of the bowel, as viewed by sigmoidoscopy, is not typical of non-specific ulcerative colitis and no amebae are found in the stools, antiamebic therapy may be worth a trial. More important in those cases in which lesions atypical of ulcerative colitis are disclosed by sigmoidoscopy, is to institute additional and more careful search for amebae. We have been gratified to find these organisms by additional examinations in several such cases. Allergy, which Dr. Rowe will discuss, is certainly a factor in many cases of ulcerative colitis, particularly in causing progression and in maintaining activity. However, I do not believe allergy is the basic or fundamental cause of the disease. The bland qualities of the diet given in determining allergic factors may be significant in the improvement noted, at least in some of the milder cases. In severe fulminating cases with almost complete anorexia, it is difficult to supply adequate calories, and for that reason such diets are contraindicated in those circumstances. In less severe cases, the patient himself will rebel at such a diet for a prolonged period. After ileostomy most patients make a striking improvement even though the colon (which the allergist considers the shock organ in ulcerative colitis) is still in the body and the patient is taking an unrestricted diet.

Miscellaneous procedures of all kinds have been used. Martin has tried using thiouracil without any truly rational basis, but with reported good results.

As to the prognosis of this disease, the best review in the literature is that of Kiefer. He reported 327 patients treated for a period of two years or over. The striking thing is the close correlation between the effectiveness of medical treatment and the amount of involvement in the bowel. Where only the rectosigmoid or this area and the left side of the bowel were involved, about two-thirds of the patients got along satisfactorily on medical treatment. On the other hand, if the entire bowel was involved, or if segmental colitis was present involving the right side of the bowel, the disease was controlled by medical management in only about one-third of the patients. Of the total patients in his series, about one-half responded satisfactorily to medical management. For patients who do not respond well to medical treatment, the choice lies between a great deal of disability and operation, which usually means ileostomy with or without colectomy.

I believe there is no great difference of opinion as to the necessity for operation in quite a large number of these patients. However, there is considerable difference of opinion as to when medical measures should be abandoned for surgical procedure and as to whether or not operation should ever be done in the patient with ulcerative colitis of the acute fulminating type. Cattell's review of the fatalities in patients undergoing operation for ulcerative colitis showed that two-thirds of the mortality came in operations done as emergency measures on these patients. The Lahey Clinic group succeeded in cutting down this mortality by getting the patient and the doctor to accept ileostomy earlier. Certainly this will decrease the mortality rate in the acute febrile cases, but it may also increase the number of patients with a permanent ileostomy who might otherwise have had a remission without it. Bargen recently stated that he and his associates at the Mayo Clinic have not had an ileostomy done for acute fulminating ulcerative colitis in the last ten years, because of the high mortality. Bockus has also abandoned use of ileostomy in the acute fulminating cases because of the associated high mortality.

Allergic Aspects

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When an allergic state is the sole cause of ulcerative colitis, pathological changes in the colon with resultant symptoms gradually disappear with the control of food, pollen or drug allergies. But when the allergic reactivity is complicated by infection, anemia, hypoproteinemia or avitaminosis, the various complications of severe or fulminating cases arise.

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Following are the reasons for considering allergic reactions to food as a primary cause of the disease:

1. Allergic reaction to foods in the gastrointestinal tract is very common. It may be localized to any area from the mouth to the anus. Allergic states in the mouth and pharynx (especially those causing canker sores), in the stomach and probably in the small intestine, have occurred not infrequently in our controlled cases of chronic ulcerative colitis. Evidence also increases that "mucous colitis," the irritable colon, colonic pain and soreness, idiopathic bleeding especially in childhood, constipation and diarrhea, as well as localized inflammations in the lower bowel, rectum and anal canal, and pruritus ani, require the proper study of allergic reactions, especially to foods, along with other recognized causes. Milk and, less frequently, fruits, egg, chocolate and other foods may cause allergic diarrhea. With recognition of such allergic states, the necessity of assuming psychosomatic causes for gastrointestinal disease, and especially symptoms, will be greatly reduced.

2. Allergic reaction offers the most logical explanation for the underlying lesions of chronic ulcerative colitis. Remembering that atopic allergic states may cause vascular reactions, the hyperemia, edema and easy bleeding of the mucosa can be understood. The granular appearance can be explained, as in atopic eczema, by the minute amounts of serum that exude from the allergically inflamed tissues, giving the mucosa a granular appearance. Protein-rich serum finally exudes, often in large amounts, causing in part the hypoproteinemia.

The herpetic and larger ulcers in the colon of many patients with ulcerative colitis may arise from minute vascular thromboses similar to those which cause oral canker sores, which as we know are usually caused by allergic reactions to food and at times to drugs or bacteria. When secondary infections occur, these ulcers extend, encouraging further infection. This infection, and especially autodigestion by trypsin rushed into the colon by hyperperistalsis, causes denudation of the mucosa and exposure of larger vessels, with consequent free or massive bleeding and at times perforation.

3. As has been shown experimentally and clinically, chronic allergic reaction can produce scar tissue. This, with or without secondary infection, can result in fibrosis, with resultant narrowing, loss of haustra, and kinks and strictures in the colon. When infection is active, fistulae, adhesions, localized or generalized peritonitis, and at times death, may result.

4. Exacerbations in chronic ulcerative colitis can be explained by the tendency for chronic allergic states to become refractory, which accounts for the recurrent attacks of bronchial asthma, allergic headaches or migraine and other manifestations, due especially to allergy to foods.

In the treatment of chronic ulcerative colitis, the possibility of allergic reaction as a cause has been considered in all our patients. For the study of possible allergic response to foods, the fruit and cereal-free elimination diet is preferred in mild or moderate cases of this disease. If the patient knows that a food in the diet disagrees, it is excluded. At first, specified vegetables may be pureed if diarrhea is marked. Potato or tapioca caramel puddings, potato-soy bakery products, and sugar with specified meats must be taken in amounts to protect weight and nutrition. In fulminating cases a "minimal diet" containing white potato, tapioca and at times rice, sugar, lamb, tea and salt may be helpful. It should contain 2,500 or more calories and at least 75 grams of protein. In those cases in which the patient is benefited, improvement occurs in about 10 to 20 days. After this is assured, then single foods such as rice, rye and corn can be added, one every five to seven days. Fruits should be tried cautiously; and milk, because of the great frequency of allergic reaction to milk in these cases, should be excluded for many months. If definite evidence of allergic response to milk or other foods is obtained, it may be wise to exclude them for years.

If allergic reaction to pollen is indicated by the patient's history, with or without positive skin tests, desensitization is important, and the use of a pollen filter in the bedroom may be advisable. In one patient with chronic ulcerative colitis that had recurred for seven years in the late summer and fall, the disease now has been well controlled with pollen antigen therapy alone for seven years. When allergic reaction to pollen is suspected, multiple antigens should be used. Extremely weak dilutions are advisable during the pollen season. Prolonged perennial desensitization is important.

For hypoproteinemia, transfusions and at times plasma are important. Amino acids by vein may be given, but the tendency to venous thromboses and reactions from them should be borne in mind. Because of the residual traces of milk or pork allergens in the trypsin digested product, the acid hydrolyzed amino acids are preferable for patients with chronic ulcerative colitis. These amino acids may be given also by mouth if the taste is tolerated.

Antihistaminic drugs have reduced cramping and tenesmus in three patients. Mild symptoms in one patient were controlled with pyribenzamine three times a day even with gradual reinstatement of a general diet.

Surgical Aspects

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We are all in agreement that the treatment of chronic ulcerative colitis is medical as long as the patient is doing well and as long as satisfactory results are obtained.

The surgeon has this to say: Many patients with ulcerative colitis die of the disease. A mistake that surgeons have made in this clinic has been in operating on patients too late. Among those patients who come to surgical operation moribund or close to

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being moribund, the mortality rate is very high. Some of these patients present surgical problems. The internist should call in the surgeon when certain problems arise, even though the patient does not require an operation. In border-line groups there may be great difficulty in arriving at a decision.

Everett Kiefer of the Lahey Clinic reported a series of late clinical results in patients with ulcerative colitis who were under medical management. In patients they treated over a period of two years, he reported good control or good results in 34 per cent; fair control in 12 per cent; and poor control in about 54 per cent. It takes a long period of time before one can draw up a lifetime prognosis of an individual patient. Histories may differ tremendously among cases. In spite of the sigmoidoscopic examination the clinical aspects may vary. Many patients have had acute or chronic ulcerative colitis and have had complete disappearance of symptoms or a long phase of remission followed by recurrence. Often the disease progresses and the patient's condition becomes worse in spite of anything that is done; and in many patients who have acute fulminating ulcerative colitis the problem is grave with or without any surgical treatment. Unless we can ear-mark each case, it is difficult to arrive at a prognosis and difficult to evaluate therapy.

There are certain indications for surgical operation: Disability from the disease in spite of any therapy; sepsis of one type or another; persistent inflammation in the colon; intra-abdominal abscesses; and inflammatory tumors of the bowel or mesentery. There is another group in which carcinoma develops—3 per cent of all patients with ulcerative colitis and 7 per cent of those operated on.

In the group reported by Kiefer, 36 per cent required surgical treatment. Cattell from the same clinic reported that in a 20-year period surgical operation was necessary for about 25 per cent of patients with ulcerative colitis. These percentage figures may be relatively high, since many of the patients were sent to the Lahey Clinic specifically for that purpose.

Ileostomy is the required procedure, and surgical deaths are experienced mainly in the first operation. Whereas the over-all mortality rate was about 20 per cent in the Lahey Clinic series, in the last two years it has been only 4 per cent—mainly because patients have been operated on earlier in the course of the disease and operation has not been carried out on patients with acute fulminating colitis.

Pseudopolyposis and fistulae as well as organic stricture in the bowel (which it is important to differentiate from spasm) are indications for surgical operation.

Many patients will have a single or recurrent severe hemorrhage from the bowel which may even cause death. During the active hemorrhage phase it is generally felt that operation is not indicated because it is impossible to determine the source of bleeding. There are, however, reports in the literature of removal of parts of the colon, during hemorrhage, with survival of the patient.

In the segmental type of ulcerative colitis as described by Crohn, involving the right or left colon, one may be able to remove the involved part and anastomose the two ends, thus preserving the continuity of the intestinal tract. Usually the rectum is involved early in the disease, which necessitates ileostomy. With the use of a new type of ileostomy bag, many of the patients have less difficulty subsequently. The Rutzen bag, custom-made for the patient, fits snugly around the ileostomy opening. It is changed twice a day and it can be drained through a spigot at the bottom.

As ileostomy is a life-saving procedure followed by return to health, we have not yet encountered a patient who would rather be as he was before the operation, despite the inconvenience. Some physicians feel that if the patient is doing well after ileostomy, it is not necessary to remove the colon later. However, many patients continue to have infection in the colon even after diversion of the fecal stream by ileostomy. They may have sepsis involving the mesentery of the colon with absorption into the portal system carried to the liver. If the colon is not removed, some patients will have stricture or malignant growth after ileostomy is performed. For these reasons it is well to remove the colon six months after ileostomy. Since there is little possibility that the ileostomy may be closed at some later time and the continuity of the bowel restored, there is little reason to preserve the colon with that in view; the patients operated upon usually have irreparable changes that have been caused by the disease.

In recent years there has been a good deal of speculation regarding emotional factors as a possible cause of ulcerative colitis, but the reports in the literature are not very convincing. Many psychiatrists who write on the subject lump all the disurbances of the colon into one category. There is a great deal of difference between a patient who has a functional disturbance of the colon and one who has ulcerative colitis. Very few gastroenterologists have seen a functional disturbance, such as irritable colon, develop ultimately into ulcerative colitis.